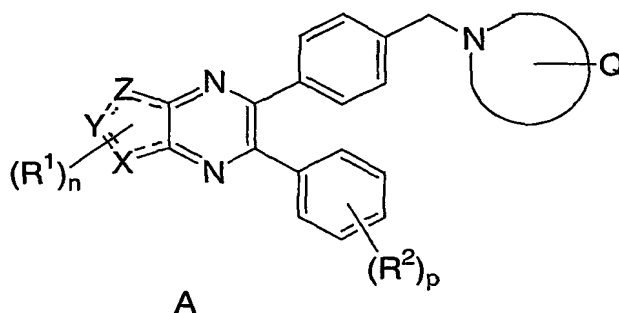


WHAT IS CLAIMED IS:

1. A compound of the formula A:



- 5 wherein:

n is 0, 1, 2 or 3;

p is 0, 1, 2 or 3;

r is 0 or 1;

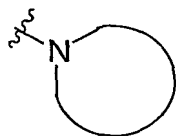
- 10 s is 0 or 1;

m is 0 or 1;

a is 0 or 1;

b is 0 or 1;

- 15 X, Y and Z are independently selected from: C, N, S or O provided that at least one of X, Y or Z is N, S or O;



is: heterocycle, optionally substituted with one to three R^Z;

- 20 Q is selected from: H, -NR⁵R⁶ and heterocycle, said heterocycle which is optionally substituted with one to three R^Z;

R¹ and R² are independently selected from:

- 25 1) (C=O)_aO_bC₁-C₁₀ alkyl,
2) (C=O)_aO_baryl,

- 3) C₂-C₁₀ alkenyl,
- 4) C₂-C₁₀ alkynyl,
- 5) (C=O)_aO_b heterocyclyl,
- 6) (C=O)_aO_bC₃-C₈ cycloalkyl,
- 5 7) CO₂H,
- 8) halo,
- 9) CN,
- 10) OH,
- 11) O_bC₁-C₆ perfluoroalkyl,
- 10 12) O_a(C=O)_bNR³R⁴,
- 13) NR^c(C=O)NR³R⁴,
- 14) S(O)_mR^a,
- 15) S(O)₂NR³R⁴,
- 16) NR^cS(O)_mR^a,
- 15 17) oxo,
- 18) CHO,
- 19) NO₂,
- 20) NR^c(C=O)O_bR^a,
- 21) O(C=O)O_bC₁-C₁₀ alkyl,
- 20 22) O(C=O)O_bC₃-C₈ cycloalkyl,
- 23) O(C=O)O_baryl, and
- 24) O(C=O)O_b-heterocycle,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R^z;

25

R³ and R⁴ are independently selected from:

- 1) H,
- 2) (C=O)_aO_bC₁-C₁₀ alkyl,
- 3) (C=O)_aO_baryl,
- 30 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) (C=O)_aO_b heterocyclyl,
- 7) (C=O)_aO_bC₃-C₈ cycloalkyl,
- 8) OH,

- 9) C₁-C₆ perfluoroalkyl,
- 10) S(O)_mR^a, and
- 11) CHO,

5 said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R^Z, or

R³ and R⁴ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in addition to the nitrogen, 1-3 heteroatoms selected from N, O and S, said
 10 monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R^Z;

R⁵ and R⁶ are independently selected from:

- 1) H,
- 15 2) (C=O)_aO_bC₁-C₁₀ alkyl,
- 3) (C=O)_aO_baryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) (C=O)_aO_b heterocyclyl,
- 20 7) (C=O)_aO_bC₃-C₈ cycloalkyl,
- 8) OH,
- 9) C₁-C₆ perfluoroalkyl,
- 10) (C=O)NR³R⁴,
- 11) S(O)_mR^a,
- 25 12) S(O)₂NR³R⁴, and
- 13) CHO,

said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R^Z, or

30 R⁵ and R⁶ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in addition to the nitrogen, 1-3 heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R^Z;

R^Z is selected from:

- 1) (C=O)_rO_s(C₁-C₁₀)alkyl,
- 2) O_r(C₁-C₃)perfluoroalkyl,
- 5 3) (C₀-C₆)alkylene-S(O)_mR^a,
- 4) oxo,
- 5) OH,
- 6) halo,
- 7) CN,
- 10 8) (C=O)_rO_s(C₂-C₁₀)alkenyl,
- 9) (C=O)_rO_s(C₂-C₁₀)alkynyl,
- 10) (C=O)_rO_s(C₃-C₆)cycloalkyl,
- 11) (C=O)_rO_s(C₀-C₆)alkylene-aryl,
- 12) (C=O)_rO_s(C₀-C₆)alkylene-heterocyclyl,
- 15 13) (C=O)_rO_s(C₀-C₆)alkylene-N(R^b)₂,
- 14) C(O)R^a,
- 15) (C₀-C₆)alkylene-CO₂R^a,
- 16) C(O)H,
- 17) (C₀-C₆)alkylene-CO₂H,
- 20 18) C(O)N(R^b)₂,
- 19) S(O)_mR^a,
- 20) NR^c(C=O)O_bR^a,
- 21) O(C=O)O_bC₁-C₁₀ alkyl,
- 22) O(C=O)O_bC₃-C₈ cycloalkyl,
- 25 23) O(C=O)O_baryl, and
- 24) O(C=O)O_b-heterocycle,

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

30

R^a is substituted or unsubstituted (C₁-C₆)alkyl, substituted or unsubstituted (C₂-C₆)alkenyl, substituted or unsubstituted (C₂-C₆)alkynyl, substituted or unsubstituted (C₃-C₆)cycloalkyl, substituted or unsubstituted aryl, (C₁-C₆)perfluoroalkyl, 2,2,2-trifluoroethyl, or substituted or unsubstituted heterocyclyl; and

R^b is H, (C₁-C₆)alkyl, substituted or unsubstituted aryl, substituted or unsubstituted benzyl, substituted or unsubstituted heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl or S(O)₂R^a;

5

R^c is selected from:

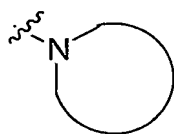
- 1) H,
- 2) C₁-C₁₀ alkyl,
- 3) aryl,
- 10 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) heterocyclyl,
- 7) C₃-C₈ cycloalkyl,
- 8) C₁-C₆ perfluoroalkyl,

15 said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R^z;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

20 2. The compound according to Claim 1 wherein:

n is 0 or 1;



25 is: heterocycle selected from 2-azepinone, benzimidazolyl, benzimidazolonyl, 2-diazapinone, imidazolyl, 2-imidazolidinone, indolyl, isoquinolinyl, morpholinyl, piperidyl, piperazinyl, pyridyl, pyrrolidinyl, 2-piperidinone, 2-pyrimidinone, 2-pyrrolidinone, quinolinyl, tetrahydrofuryl, tetrahydroisoquinolinyl, and thienyl, said heterocycle optionally substituted with one to three R^z;

30

Q is selected from: H and -NR⁵R⁶;

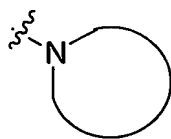
R¹ and R² are independently selected from:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl,
- 2) (C=O)_aO_baryl,
- 3) C₂-C₁₀ alkenyl,
- 4) C₂-C₁₀ alkynyl,
- 5) (C=O)_aO_b heterocyclyl,
- 6) (C=O)_aO_bC₃-C₈ cycloalkyl,
- 7) CO₂H,
- 8) halo,
- 9) CN,
- 10) OH,
- 11) O_bC₁-C₆ perfluoroalkyl,
- 12) S(O)_mR^a,
- 13) NR^cS(O)_mR^a,
- 14) oxo,
- 15) CHO,
- 16) NO₂,
- 17) NR^c(C=O)O_bR^a,
- 18) O(C=O)O_bC₁-C₁₀ alkyl,
- 19) O(C=O)O_bC₃-C₈ cycloalkyl,
- 20) O(C=O)O_baryl,
- 21) O(C=O)O_b-heterocycle, and
- 22) NH₂,

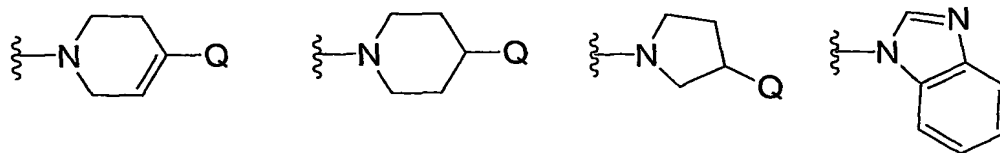
said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R^z;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

3. The compound according to Claim 2 wherein:



is: heterocycle selected from



said heterocycle optionally substituted with one to three R^Z ;

5 Q is selected from: $-NR^5R^6$;

R^5 and R^6 are independently selected from:

- 1) H,
- 2) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 10 3) $(C=O)_aO_b$ aryl,
- 4) C_2-C_{10} alkenyl,
- 5) C_2-C_{10} alkynyl,
- 6) $(C=O)_aO_b$ heterocyclyl,
- 7) $(C=O)_aO_bC_3-C_8$ cycloalkyl,
- 15 8) OH,
- 9) C_1-C_6 perfluoroalkyl,
- 10) $S(O)_mR^a$, and
- 11) CHO,

20 said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R^Z , or

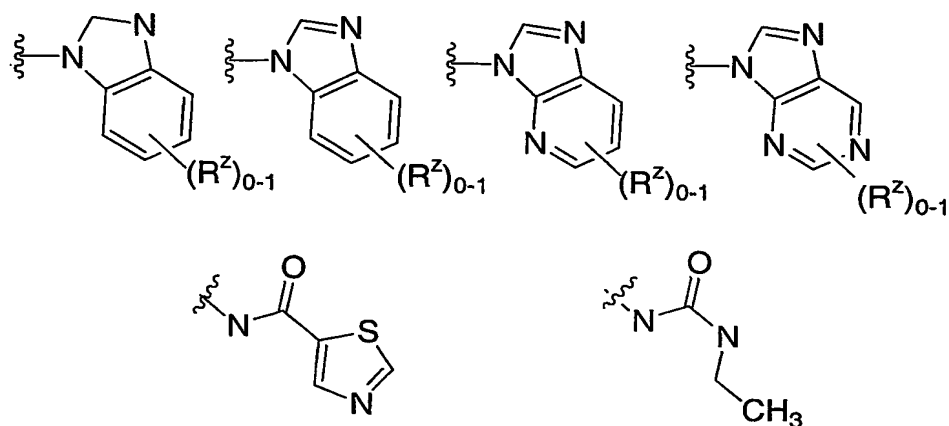
R^5 and R^6 can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in addition to the nitrogen, 1-3 heteroatoms selected from N, O and S, said
25 monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R^Z ;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

30

4. The compound according to Claim 3 wherein:

Q is selected from:



wherein R^Z can attach anywhere on the bicyclic structure;

5

R^1 and R^2 are independently selected from:

- 1) (C_1-C_6) alkyl,
- 2) (C_1-C_{10}) alkyl-OH
- 3) CO_2H ,
- 10 4) halo,
- 5) CN,
- 6) OH,
- 7) oxo,
- 8) CHO,
- 15 9) NO_2 , and
- 10) NH_2

R^Z is independently selected from:

- 1) (C_1-C_6) alkyl,
- 20 2) (C_1-C_{10}) alkyl-OH
- 3) CO_2H ,
- 4) halo,
- 5) CN,
- 6) OH,
- 25 7) oxo,
- 8) CHO,

- 9) NO₂, and
 10) NH₂

or a pharmaceutically acceptable salt or a stereoisomer thereof.

5

5. A compound which is selected from:

- 1- $\{1-[4-(3\text{-phenylthieno}[3,4\text{-}b]\text{pyrazin-2-yl})\text{benzyl}]\text{piperidin-4-yl}\}$ -1,3-dihydro-2*H*-
 10 benzimidazol-2-one;
N-ethyl-*N'*- $\{(3R)\text{-}1-[4-(3\text{-phenylthieno}[3,4\text{-}b]\text{pyrazin-2-yl})\text{benzyl}]\text{pyrrolidin-3-yl}\}$ urea;
 15 *N*- $\{(3R)\text{-}1-[4-(3\text{-phenylthieno}[3,4\text{-}b]\text{pyrazin-2-yl})\text{benzyl}]\text{pyrrolidin-3-yl}\}$ -1,3-thiazole-5-carboxamide;
 9- $\{1-[4-(3\text{-phenylthieno}[3,4\text{-}b]\text{pyrazin-2-yl})\text{benzyl}]\text{piperidin-4-yl}\}$ -9*H*-purin-6-amine;
 20 2-(4- $\{[4-(3*H*\text{-imidazo}[4,5\text{-}b]\text{pyridin-3-yl})\text{piperidin-1-yl}]\text{methyl}\}$ phenyl)-3-phenylthieno[3,4-*b*]pyrazine;
 9- $\{1-[4-(3\text{-phenylthieno}[3,4\text{-}b]\text{pyrazin-2-yl})\text{benzyl}]\text{piperidin-4-yl}\}$ -9*H*-purine;
 25 $\{1-[4-(3\text{-phenylthieno}[3,4\text{-}b]\text{pyrazin-2-yl})\text{benzyl}]\text{-}1*H*\text{-benzimidazol-2-yl}\}$ methanol;
 2- $\{4-[(2\text{-methyl-}1*H*\text{-benzimidazol-1-yl})\text{methyl}]\text{phenyl}\}$ -3-phenylthieno[3,4-*b*]pyrazine;
 30 1- $\{1-[4-(3\text{-phenylthieno}[3,4\text{-}b]\text{pyrazin-2-yl})\text{benzyl}]\text{-}1,2,3,6\text{-tetrahydropyridin-4-yl}\}$ -1,3-dihydro-2*H*-benzimidazol-2-one;
N- $\{(3R)\text{-}1-[4-(3\text{-hydroxy-5-phenyl-2*H*\text{-pyrazolo}[3,4\text{-}b]\text{pyrazin-6-yl})\text{benzyl}]\text{pyrrolidin-3-yl}\}$ -1,3-thiazole-5-carboxamide; and

1-{1-[4-(3-hydroxy-5-phenyl-2*H*-pyrazolo[3,4-*b*]pyrazin-6-yl)benzyl]piperidin-4-yl}-1,3-dihydro-2*H*-benzimidazol-2-one;

5 or a pharmaceutically acceptable salt or a stereoisomer thereof.

6. The TFA salt of a compound according to Claim 1 which is:

10 1-{1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]piperidin-4-yl}-1,3-dihydro-2*H*-benzimidazol-2-one;

N-ethyl-*N'*-(3*R*)-1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]pyrrolidin-3-yl}urea;

15 *N*-(3*R*)-1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]pyrrolidin-3-yl}-1,3-thiazole-5-carboxamide;

9-{1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]piperidin-4-yl}-9*H*-purin-6-amine;

20 2-(4-{[4-(3*H*-imidazo[4,5-*b*]pyridin-3-yl)piperidin-1-yl]methyl}phenyl)-3-phenylthieno[3,4-*b*]pyrazine;

9-{1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]piperidin-4-yl}-9*H*-purine;

25 {1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]-1*H*-benzimidazol-2-yl}methanol;

2-{4-[(2-methyl-1*H*-benzimidazol-1-yl)methyl]phenyl}-3-phenylthieno[3,4-*b*]pyrazine;

30 1-{1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]-1,2,3,6-tetrahydropyridin-4-yl}-1,3-dihydro-2*H*-benzimidazol-2-one;

N-(3*R*)-1-[4-(3-hydroxy-5-phenyl-2*H*-pyrazolo[3,4-*b*]pyrazin-6-yl)benzyl]pyrrolidin-3-yl}-1,3-thiazole-5-carboxamide; and

35

1-{1-[4-(3-hydroxy-5-phenyl-2*H*-pyrazolo[3,4-*b*]pyrazin-6-yl)benzyl]piperidin-4-yl}-
1,3-dihydro-2*H*-benzimidazol-2-one;

or a stereoisomer thereof.

5

7. A compound according to Claim 5 which is selected from:

1-{1-[4-(3-phenylthieno[3,4-*b*]pyrazin-2-yl)benzyl]piperidin-4-yl}-1,3-dihydro-2*H*-
benzimidazol-2-one;

10

or a pharmaceutically acceptable salt or a stereoisomer thereof.

8. A pharmaceutical composition comprising a pharmaceutical
15 carrier, and dispersed therein, a therapeutically effective amount of a compound of
Claim 1.

9. A pharmaceutical composition comprising a pharmaceutical
carrier, and dispersed therein, a therapeutically effective amount of a compound of
20 Claim 6.

10. A method of inhibiting one or more of the isoforms of Akt in a
mammal which comprises administering to the mammal a therapeutically effective
amount of a compound of Claim 1.

25

11. A method of inhibiting one or more of the isoforms of Akt in a
mammal which comprises administering to the mammal a therapeutically effective
amount of a compound of Claim 6.

12. A method for treating cancer which comprises administering to
30 a mammal in need thereof a therapeutically effective amount of a compound of Claim
1.

13. A method for treating cancer which comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 6.

5 14. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

10 15. A process for making a pharmaceutical composition comprising combining a compound of Claim 1 and a pharmaceutically acceptable carrier.

16. The composition of Claim 8 further comprising a second compound selected from:

- 15 1) an estrogen receptor modulator,
2) an androgen receptor modulator,
3) retinoid receptor modulator,
4) a cytotoxic agent,
5) an antiproliferative agent,
6) a prenyl-protein transferase inhibitor,
20 7) an HMG-CoA reductase inhibitor,
8) an HIV protease inhibitor,
9) a reverse transcriptase inhibitor,
10) an angiogenesis inhibitor,
11) an inhibitor of inherent multidrug resistance,
25 12) an anti-emetic agent,
13) an agent useful in the treatment of anemia,
14) agent useful in the treatment of neutropenia, and
15) an immunologic-enhancing drug.

30 17. The composition of Claim 16, wherein the second compound is an angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP inhibitor, an integrin blocker, interferon- α , interleukin-12, pentosan polysulfate, a

cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-(chloroacetyl-carbonyl)-fumagillol, thalidomide, angiostatin and troponin-1.

18. The composition of Claim 16, wherein the second compound is
5 an estrogen receptor modulator selected from tamoxifen and raloxifene.

19. A method of treating cancer which comprises administering a
therapeutically effective amount of a compound of Claim 1 in combination with
radiation therapy.

10

20. A method of treating or preventing cancer which comprises
administering a therapeutically effective amount of a compound of Claim 1 in
combination with a compound selected from:

- 15
- 1) an estrogen receptor modulator,
 - 2) an androgen receptor modulator,
 - 3) retinoid receptor modulator,
 - 4) a cytotoxic agent,
 - 5) an antiproliferative agent,
 - 6) a prenyl-protein transferase inhibitor,
 - 20 7) an HMG-CoA reductase inhibitor,
 - 8) an HIV protease inhibitor,
 - 9) a reverse transcriptase inhibitor,
 - 10) an angiogenesis inhibitor,
 - 11) an inhibitor of inherent multidrug resistance,
 - 25 12) an anti-emetic agent,
 - 13) an agent useful in the treatment of anemia,
 - 14) agent useful in the treatment of neutropenia, and
 - 15) an immunologic-enhancing drug.

30 21. A method of treating cancer which comprises administering a
therapeutically effective amount of a compound of Claim 1 in combination with
radiation therapy and a compound selected from:

- 35
- 1) an estrogen receptor modulator,
 - 2) an androgen receptor modulator,
 - 3) retinoid receptor modulator,

- 5
- 10
- 4) a cytotoxic agent,
 - 5) an antiproliferative agent,
 - 6) a prenyl-protein transferase inhibitor,
 - 7) an HMG-CoA reductase inhibitor,
 - 8) an HIV protease inhibitor,
 - 9) a reverse transcriptase inhibitor,
 - 10) an angiogenesis inhibitor,
 - 11) an inhibitor of inherent multidrug resistance,
 - 12) an anti-emetic agent,
 - 13) an agent useful in the treatment of anemia,
 - 14) agent useful in the treatment of neutropenia, and
 - 15) an immunologic-enhancing drug.

- 15
22. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.